Development of Ultrasonic-Measurement-Integrated Simulation of Real Blood Flows for Diagnosis of Circulatory Diseases

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論文内容要旨

Chapter 1　Introduction

Circulatory diseases have been investigated experimentally and numerically in order to elucidate the cause and to develop methods for diagnosis and treatment of them. For those investigations, hemodynamic information is essential. However, existing methods in experimental measurement and numerical simulation have individual limitations. In order to overcome the problems in obtaining detailed and accurate information of blood flows, we have investigated the integration of ultrasonic Doppler measurement and numerical simulation based on the concept of the flow observer (see Fig. 1). We call this novel blood flow analysis method *Ultrasonic-Measurement-Integrated (UMI) simulation.*

Chapter 2　Ultrasonic-Measurement-Integrated (UMI) simulation

Chapter 2 introduced the composition of UMI simulation. The primary components of the UMI simulation; i.e. ultrasonic diagnostic equipment and numerical simulation, were first reviewed. And then, UMI simulation was formulated by providing the detailed fundamental equations of the numerical simulation.

UMI simulation constructs a simulation model of blood flow with feedback algorithm in a computer using a standard computational method based on the SIMPLER method that solves fundamental equations with assumed boundary and initial conditions. Error of the model is evaluated by comparing some output signals obtained by the real flow measurement and the corresponding computational results, and is modified with the aid of feedback. For the feedback, an artificial force proportional to the optimum estimation of the difference between the measured and computed velocity vectors obtained from the Doppler velocities is added to the numerical simulation as a feedback signal at each feedback point. The feedback points are defined at some grid points in a feedback domain which is a subset of the computational domain in which the measurement data can be obtained.

Toward the application of UMI simulation to real blood flow analysis, feedback formulae were designed to deal with lacks of the measurement data. In addition, methods for detecting and correcting aliasing, which supplies incorrect magnitude and opposite direction of Doppler velocities and may lead UMI simulation to wrong results, were proposed. Feedback signals inevitably influence the pressure in UMI simulation and possibly cause deviance from the real pressure. Additional pressure correction method was presented for UMI simulation.

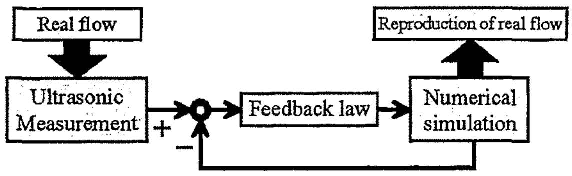


Fig. 1 Schematic diagram of UMI simulation.

Chapter 3 Preliminary two-dimensional blood flow analysis

The validity of UMI simulation was numerically investigated in Chapter 3 using a two-dimensional model problem of blood flow in an aneurysmal aorta. The work first defined two rectangular feedback domains, which covered an aneurysm or the blood vessel around the aneurysm. Feedback signals were applied at feedback points which were defined at all grid points or at dispersed points changing its interval or density in those feedback domains. In addition, the feedback domain was moved upstream or downstream. The results obtained in the numerical experiment revealed the fundamental characteristics of UMI simulation.

The application of an artificial force to the governing equations to compensate for error in the Doppler velocity between numerical simulation and standard solution reduces the error both in velocity and pressure in comparison with ordinary simulation. Especially, the error of velocity significantly decreases in the feedback domain.

The computational accuracy of UMI simulation is sensitive to the feedback gain. The optimal feedback gain was investigated using the average error norm of velocity vector as an objective function, but it might be determined by the average error norm of Doppler velocity.

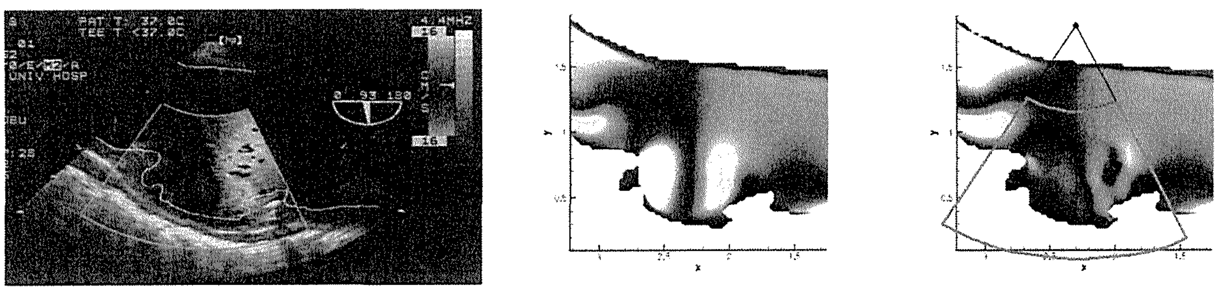
The error of UMI simulation decreases with increasing density of feedback points in the domain, but it becomes less sensitive for larger value of the density. Though a locally concentrated arrangement of feedback points in the targeted domain intensively improves the computational accuracy in that part, it is also affected by the error surrounding the region. Therefore, it is probably better to arrange a somewhat large feedback domain that includes the targeted region.

The effect of feedback also appears outside the feedback domain. Except for the case using a feedback domain located near the downstream boundary, the error in the velocity field decreases starting just before the feedback domain, continuing through it and persisting for some distance in the downstream region. Concerning the pressure field, feedback generates an adverse effect in the UMI simulations whose feedback domains are located near upstream or downstream boundaries. Hence, the feedback point arrangement near upstream and downstream boundaries should be avoided.

The UMI simulation requires some additional computational time for feedback, but enhancement of convergence to the final solution results in a reduction in total computational time. Consequently, the overall computational time necessary to obtain periodic solution is substantially reduced with increasing density of the feedback points due to a reduction of number of time steps.

Artificial introduction of aliasing to the standard numerical solution caused UMI simulation to differ from the standard solution and the error became greater than that of the ordinary numerical simulation. In order to eliminate the effect of aliasing, the artificial force in the feedback of the UMI simulation can be used as an excellent index to detect the aliasing. After detecting aliasing, correction A, in which measurement velocity is replaced with the computational one at the feedback point where the aliasing is detected, substantially improves the accuracy of UMI simulation. Correction B, in which measurement velocity is replaced with an estimated Doppler velocity at the point, provides exactly the same result as that of the UMI simulation using the nonaliased standard solution.

As final investigation for the two-dimensional problem, UMI simulation with real color Doppler imaging was performed and showed good agreement with the measurement (see Fig. 2). Both correction method A and B were used in UMI simulation against aliasing in real color Doppler images. Though correction B yields the most accurate result in the numerical experiment, it is strongly affected by measurement noise. In contrast, correction A is more robust and, therefore, would be a better choice considering the presence of artifacts in the measurement.



(a) Measurement data (b) Ordinary simulation (c) UMI simulation

Fig. 2 Comparison of color Doppler images.

Chapter 4 Evaluation of UMI simulation with three-dimensional steady blood flow analysis

Chapter 4 dealt with a numerical experiment of UMI simulation with a steady standard solution of the three-dimensional blood flow in an aneurysmal aorta with a realistic boundary condition. The transient and steady characteristics of UMI simulation, which determine the convergence to the target flow as well as the frequency response to the oscillatory blood flows, were first investigated by observing variation of the error derived from the inaccurate boundary conditions in the velocity field in the aneurysm. The UMI simulation was performed assuming the acquisition of Doppler velocities in the aneurysmal domain by color Doppler imaging using one ultrasound probe or multiple probes. Feedback signals proportional to the optimal estimation of the difference of velocity vector obtained by the Doppler velocities against the standard solution were applied at all grid points in the feedback domain. The obtained characteristics of the UMI simulation are summarized as follows.

UMI simulation requires time-dependent calculation even for a steady target flow, and is independent of the time increment Δt if Δt is smaller than some critical value. However, it suddenly diverges if Δt is larger than the critical value. The critical time increment is inversely proportional to the feedback gain.

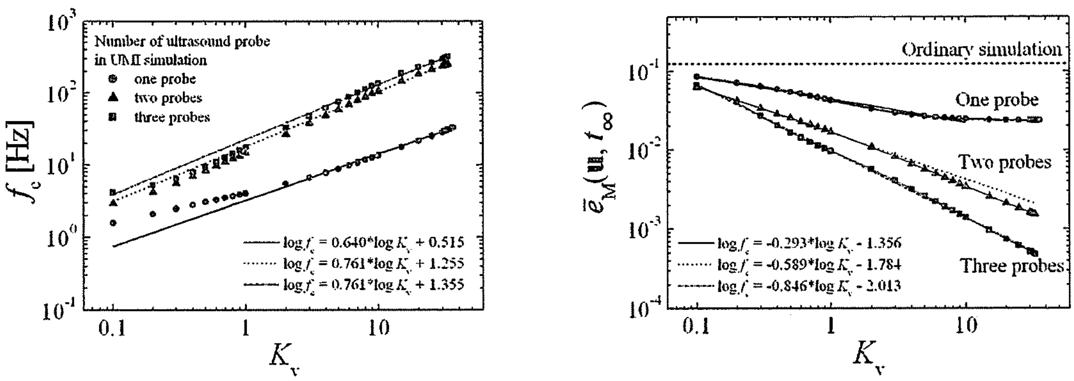
As time progresses, the application of feedback exponentially reduces the error in the velocity field due to an inaccurate boundary condition in and after the feedback domain, and makes it converge to a steady state. The improvement of accuracy gradually deteriorates after the feedback domain toward the downstream boundary.

With increasing feedback gain K_v, the error decreases faster and the frequency response of UMI simulation using one probe improves to the 0.640th power of K_v, implying the ability to follow the real blood flow oscillation at large K_v [see Fig. 3 (a)]. By using multiple probes, the convergence to the standard solution is accelerated and the frequency response shows high enough value.

The error becomes smaller being proportional to K_v^a ($a < 0$) in UMI simulation [see Fig. 3 (b)]. But in the case of using one probe, the optimal feedback gain exists for decreasing the steady error, and a constant error independent of K_v remains for $K_v \geq 10$. Increasing the velocity error information obtained by using multiple ultrasound probes brings UMI simulation further efficient performance. Considering practical operation, UMI simulation using two probes is suitable and provides an adequate performance.

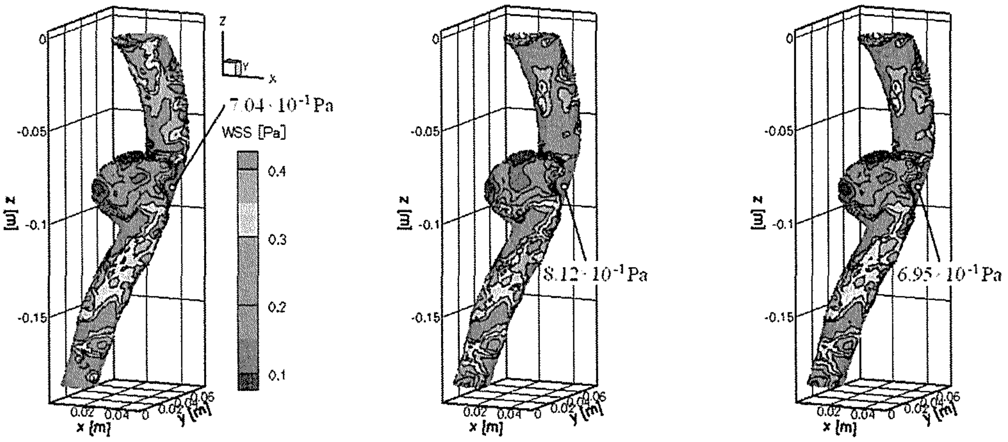
In UMI simulation using one ultrasound probe, the maximum reduction of the error is achieved by placing the probe at the same height as the aneurysm since the blood flow field recirculates in the aneurysm. But the frequency response improves as the probe is set at the downstream side of the aneurysm. Considering these characteristics, the same height as the aneurysm is regarded as the best probe position for one probe.

The effect of feedback point arrangement on three-dimensional blood flow field was investigated in two cases: (1) the feedback points were arranged in the feedback domain extended toward the upstream or both upstream and downstream starting from the aneurysmal domain, (2) the feedback points were set at discrete grid points in the aneurysmal domain at isotropic or anisotropic intervals with varying density. In order to reproduce the blood flow field in an aneurysm, extension of the feedback domain upstream from the aneurysmal domain is preferable. However, the domain should be away from the upstream and downstream boundaries. Concerning the feedback point arrangement in the feedback domain, the dense acquisition of Doppler velocities on cross-sections orthogonal to the mainstream direction is the most effective in the anisotropic arrangements because of the flow convection, and gives computational accuracy comparable to the isotropic feedback point arrangement.



(a) Cutoff frequency (b) Steady error of velocity vector

Fig. 3 Transient and steady characteristics of UMI simulations.



(a) Standard solution (b) Ordinary simulation (c) UMI simulation with one probe

Fig. 4 Time-averaged wall shear stress distribution on an aneurysmal aorta with its maximum value.

The application of feedback to the governing equations adversely affects the pressure field as well as reduces the error in the velocity field. The pressure deviance is increased in front and in the upstream side of the feedback domain. In order to estimate the real pressure field, subtraction of the pressure field derived from the divergence of feedback signals from the pressure field obtained by UMI simulation successfully eliminates the adverse effect of feedback on the pressure field.

Chapter 5 Three-dimensional unsteady blood flow analysis

In chapter 5, in order to investigate the efficiency of UMI simulation of real blood flow, a numerical experiment was performed dealing with the three-dimensional unsteady blood flow field in an aneurysm. The UMI simulation was carried out based on the knowledge acquired in the previous chapters. In performing the UMI simulation using real measurement data, insufficient time resolution of the ultrasonic measurement might be a problem. For this problem, we considered the timing of feedback. Moreover, the ability of UMI simulation was examined under the ideal condition concerning the cases that the feedback domain was set at the aneurysmal domain using one probe or two probes, and of the extended feedback domain using one probe.

The intermittent feedback method, which applies feedback signals only at timing when measurement data is obtained, provides the same computational accuracy as the UMI simulation under the ideal condition if the computation is carried out stably. Therefore, this feedback way is a possible solution for the insufficient time resolution of the ultrasonic measurement. UMI simulation with intermittent feedback has the possibility of integrating real ultrasonic Doppler measurement whose time resolution is as large as $\Delta t_{\mathrm{in}} = 0.033$ s.

Reduction of error in the three-dimensional unsteady blood flow field is achieved by UMI simulation using one or two ultrasound probes. With one probe, the errors in velocity and pressure decrease to 29% and to 58%, respectively, in the feedback domain which covers the aneurysm. Using two ultrasound probes enhances the ability. The errors in velocity and pressure become small at all time steps, and decrease to 8% and to 17%, respectively, in the feedback domain. Hence, UMI simulation can produce more reliable information of hemodynamic stresses than the ordinary simulation (see Fig. 4). Note that the ordinary simulation provides a similar blood flow field to the standard solution on the whole but sometimes shows local disagreements, which may cause a big mistake in the diagnosis of circulatory diseases.

Chapter 6 Summary

Major findings in this study were summarized in this chapter.

The potential of UMI simulation to accurately reproduce real blood flows have been validated. Based on the obtained knowledge of the transient and steady characteristics, UMI simulation of real blood flows will bring significant benefits for the clinical diagnosis and treatment of circulatory diseases: the detailed and accurate information of blood flows is provided and hemodynamic stresses are more correctly estimated than by existing methods.

論文審査結果の要旨

循環器病は、現代のわが国の主要死因の一つであり、非侵襲かつ高精度の診断方法の確立が強く望まれている。疾患の原因は血行力学にあり、診断に際しては、個々の患者の血管内血流場の正確かつ詳細な情報が必要不可欠となる。しかし、実際の血流場を再現するという目的に対し、現存する血流場の計測手法及び数値解析手法は本質的な問題点を有する。著者は、超音波計測と数値解析を融合した超音波計測融合シミュレーションを構築し、大動脈瘤内の血流解析を題材にその有用性を証明した。本論文は、この研究成果についてまとめたもので、全文6章よりなる。

第1章は序論であり、本研究の背景及び目的を述べている。

第2章では、超音波計測融合シミュレーションの構成要素である、超音波計測と数値解析について詳述し、さらに両手法を融合するフィードバック手法を論じるとともに、融合における諸問題の対応策を提示している。

第3章では、基礎的検討として2次元血流場の数値解を解析対象に、上流境界速度分布条件の差異に起因する誤差の低減に関する数値実験について論じた後、2次元領域の実際の計測データとの融合結果を示している。計測結果と計算結果の誤差のフィードバックにより、対象とする血流場の各方向の速度成分及び圧力を再現でき、また、計測誤差を排除した血流場の観察が可能となることが示された。これは超音波計測融合シミュレーションの有用性を示す重要な成果である。

第4章では、3次元定常の血流場の数値解を解析対象に、超音波計測融合シミュレーションの定常特性と過渡特性について考察している。超音波計測融合シミュレーションの解析性能は、フィードバックゲインの増大に伴い指数関数的に向上し、複数の超音波プローブを用いた速度ベクトルの誤差の最適推定に基づくフィードバックにより、十分な精度で実際の流れ場に追従できることが明らかにされた。また、フィードバック点配置を変化させ、計算領域全体に及ぶフィードバックの影響を評価するとともに、計算結果の圧力場を補正することの有効性を示した。得られた知見は、超音波計測融合シミュレーションの基本的な特性を明確にした有用な成果である。

第5章では、実際の血流場の状態である3次元非定常の血流場に対する超音波計測融合シミュレーションの有用性を、数値実験により論じている。超音波計測における時間分解能の制限は、計算時間刻みを細かく設定する一方、計測データが得られる時刻のみに間欠的にフィードバックを適用することにより克服できることが示された。これは、実際の診断における超音波計測融合シミュレーションの導入に向けた、実用上重要な成果である。

第6章は結論である。

以上要するに、本論文は新たな血流解析手法である超音波計測融合シミュレーションの有用性を明示したものであり、工学のみならず医療の発展に寄与するところが少なくない。

よって、本論文は博士(工学)の学位論文として合格と認める。